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PATENT  
ATTORNEY'S DOCKET NO.: NBG-109

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Aldo Salimbeni et al.  
Serial No.: 10/537,731  
Filed: June 6, 2005  
For: PROCESS FOR THE PREPARATION OF BICYCLIC  
PEPTIDE COMPOUNDS  
Examiner: Not Assigned  
Art Unit: Not Assigned

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CERTIFICATE OF MAILING

I hereby certify that the following correspondence is being deposited with the United States Postal service as first class mail in an envelope addressed to the Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450 on February 22, 2007.

  
Mark D. Lorusso

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Commissioner for Patents  
PO BOX 1450  
Alexandria, VA 22313-1450

**RESPONSE TO STIC BIOTECHNOLOGY SYSTEMS BRANCH**  
**RAW SEQUENCE LISTING ERROR REPORT**

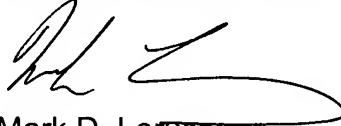
Sir:

This responds to the Raw Sequence Listing Error Report processed July 3, 2006. On February 21, 2007, applicants' counsel of record spoke with Anne-Marie Corrigan in the STIC Biotechnology Systems Branch with respect to the Raw Sequence Report and was faxed a copy of the report not previously received. Ms. Corrigan explained the substantive errors that could not be identified with the CHECKER software.

Enclosed herewith are two copies of the corrected Sequence Listing in computer readable format. Another copy of the corrected Sequence Listing in paper form is also enclosed. The content of the Sequence Listing information recorded in computer

readable form is identical to the written sequence listing and does not include any new matter. A courtesy copy of the Raw Sequence Listing Error Report is also enclosed to facilitate processing of this response.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Mark D. Lorusso', with a long horizontal flourish extending to the right.

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Lorusso & Associates  
3 Pinecrest Terrace  
Portsmouth, NH 03801  
Tel: (603) 427-0070  
Attorneys for Applicants

Docket No.: NBG-109

Date: February 22, 2007

**STIC Biotechnology Systems Branch****RAW SEQUENCE LISTING**  
**ERROR REPORT**

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/537,731  
Source: PTA  
Date Processed by STIC: 7/3/06

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE **CHECKER** **VERSION 4.4.0 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

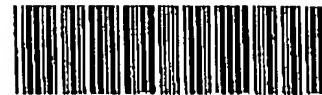
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):  
U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/10/06

## Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: 10/537,731
ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE		
1 ____ Wrapped Nucleics Wrapped Aminos	The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."	
2 ____ Invalid Line Length	The rules require that a line not exceed 72 characters in length. This includes white spaces.	
3 ____ Misaligned Amino Numbering	The numbering under each 5 <sup>th</sup> amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.	
4 ____ Non-ASCII	The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.	
5 ____ Variable Length	Sequence(s) ____ contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.	
6 ____ PatentIn 2.0 "bug"	A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) _____. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.	
7 ____ Skipped Sequences (OLD RULES)	Sequence(s) ____ missing. If intentional, please insert the following lines for each skipped sequence: (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.	
8 ____ Skipped Sequences (NEW RULES)	Sequence(s) ____ missing. If intentional, please insert the following lines for each skipped sequence. <210> sequence id number <400> sequence id number 000	
9 ____ Use of n's or Xaa's (NEW RULES)	Use of n's and/or Xaa's have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.	
10 ____ Invalid <213> Response	Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence. (see item 11 below)	
11 ____ Use of <220>	Sequence(s) ____ missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section or use "chemically synthesized" as explanation. (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32), also Sec. 1.823 of Sequence Rules	
12 ____ PatentIn 2.0 "bug"	Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.	
13 ____ Misuse of n/Xaa	"n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid	



PCT

## RAW SEQUENCE LISTING

DATE: 07/03/2006

PATENT APPLICATION: US/10/537,731

TIME: 11:56:39

Input Set : E:\3874 PTUS sequence listing.txt  
Output Set: N:\CRF4\07032006\J537731.raw

3 <110> APPLICANT: SALIMBENI, Aldo et al  
5 <120> TITLE OF INVENTION: Process for the preparation of bicyclic hexa-peptide  
nepadutant

7 <130> FILE REFERENCE: 3874PTUS  
C--> 9 <140> CURRENT APPLICATION NUMBER: US/10/537,731  
C--> 10 <141> CURRENT FILING DATE: 2005-06-06  
12 <150> PRIOR APPLICATION NUMBER: FI2002A000239  
13 <151> PRIOR FILING DATE: 2002-06-12  
15 <160> NUMBER OF SEQ ID NOS: 11  
17 <170> SOFTWARE: PatentIn version 3.3  
19 <210> SEQ ID NO: 1  
20 <211> LENGTH: 5  
21 <212> TYPE: PRT  
22 <213> ORGANISM: pentapeptide  
25 <220> FEATURE:  
26 <221> NAME/KEY: BINDING  
27 <222> LOCATION: (1)..(1)  
28 <223> OTHER INFORMATION: Asp is bound to a benzyloxycarbonyl group  
30 <220> FEATURE:  
31 <221> NAME/KEY: MISC\_FEATURE  
32 <222> LOCATION: (4)..(4)  
33 <223> OTHER INFORMATION: X is Dpr (i.e. 2,3-diaminopropionic acid)  
35 <220> FEATURE:  
36 <221> NAME/KEY: MOD\_RES  
37 <222> LOCATION: (5)..(5)  
38 <223> OTHER INFORMATION: METHYLATION  
40 <400> SEQUENCE: 1

W--&gt; 42 Asp Trp Phe Xaa Leu

43 1. 5  
46 <210> SEQ ID NO: 2  
47 <211> LENGTH: 5  
48 <212> TYPE: PRT  
49 <213> ORGANISM: Artificial Sequence  
51 <220> FEATURE: never has a vsp.  
52 <223> OTHER INFORMATION: cyclic pentapeptide  
55 <220> FEATURE:  
56 <221> NAME/KEY: BINDING  
57 <222> LOCATION: (1)..(1)  
58 <223> OTHER INFORMATION: Asp is bound to a benzyloxycarbonyl group  
60 <220> FEATURE:  
61 <221> NAME/KEY: SITE  
62 <222> LOCATION: (1)..(4)  
63 <223> OTHER INFORMATION: Asp and Dpr are bound together to form a cycle  
65 <220> FEATURE:

see  
pg 1, 6  
Does Not Comply  
Corrected Diskette Needed

invalid response -  
see item 10 on  
Error Summary Sheet

## RAW SEQUENCE LISTING

DATE: 07/03/2006

PATENT APPLICATION: US/10/537,731

TIME: 11:56:39

Input Set : E:\3874 PTUS sequence listing.txt

Output Set: N:\CRF4\07032006\J537731.raw

66 <221> NAME/KEY: MISC\_FEATURE  
67 <222> LOCATION: (4)..(4)  
68 <223> OTHER INFORMATION: X is Dpr (i.e. 2,3-diaminopropionic acid)  
70 <220> FEATURE:  
71 <221> NAME/KEY: MOD\_RES  
72 <222> LOCATION: (5)..(5)  
73 <223> OTHER INFORMATION: METHYLATION  
75 <400> SEQUENCE: 2  
W--> 77 Asp Trp Phe Xaa Leu  
78 1 5  
81 <210> SEQ ID NO: 3  
82 <211> LENGTH: 5  
83 <212> TYPE: PRT  
84 <213> ORGANISM: Artificial Sequence  
86 <220> FEATURE:  
87 <223> OTHER INFORMATION: cyclic pentapeptide  
90 <220> FEATURE:  
91 <221> NAME/KEY: BINDING  
92 <222> LOCATION: (1)..(1)  
93 <223> OTHER INFORMATION: Asp is bound to a benzyloxycarbonyl group  
95 <220> FEATURE:  
96 <221> NAME/KEY: SITE  
97 <222> LOCATION: (1)..(4)  
98 <223> OTHER INFORMATION: Asp and Dpr are bound together to form a cycle  
100 <220> FEATURE:  
101 <221> NAME/KEY: MISC\_FEATURE  
102 <222> LOCATION: (4)..(4)  
103 <223> OTHER INFORMATION: X is Dpr (i.e. 2,3-diaminopropionic acid)  
105 <400> SEQUENCE: 3  
W--> 107 Asp Trp Phe Xaa Leu  
108 1 5  
111 <210> SEQ ID NO: 4  
112 <211> LENGTH: 6  
113 <212> TYPE: PRT  
114 <213> ORGANISM: Artificial Sequence  
116 <220> FEATURE:  
117 <223> OTHER INFORMATION: cyclic hexapeptide  
120 <220> FEATURE:  
121 <221> NAME/KEY: BINDING  
122 <222> LOCATION: (1)..(1)  
123 <223> OTHER INFORMATION: Asp is bound to a benzyloxycarbonyl group and to a tert-butyl  
124 group  
126 <220> FEATURE:  
127 <221> NAME/KEY: SITE  
128 <222> LOCATION: (2)..(5)  
129 <223> OTHER INFORMATION: Asp and Dpr are bound together to form a cycle  
131 <220> FEATURE:  
132 <221> NAME/KEY: MISC\_FEATURE  
133 <222> LOCATION: (5)..(5)

## RAW SEQUENCE LISTING

DATE: 07/03/2006

PATENT APPLICATION: US/10/537,731

TIME: 11:56:39

Input Set : E:\3874 PTUS sequence listing.txt

Output Set: N:\CRF4\07032006\J537731.raw

134 <223> OTHER INFORMATION: X is Dpr (i.e. 2,3-aminopropionic acid)  
136 <400> SEQUENCE: 4  
W--> 138 Asp Asp Trp Phe Xaa Leu  
139 1 5  
142 <210> SEQ ID NO: 5  
143 <211> LENGTH: 6  
144 <212> TYPE: PRT  
145 <213> ORGANISM: Artificial Sequence  
147 <220> FEATURE:  
148 <223> OTHER INFORMATION: bicyclic hexapeptide  
151 <220> FEATURE:  
152 <221> NAME/KEY: SITE  
153 <222> LOCATION: (1)..(6)  
154 <223> OTHER INFORMATION: Asp and Leu are bound together to form a cycle  
156 <220> FEATURE:  
157 <221> NAME/KEY: BINDING  
158 <222> LOCATION: (1)..(1)  
159 <223> OTHER INFORMATION: Asp is bound to a tert-butyl group  
161 <220> FEATURE:  
162 <221> NAME/KEY: SITE  
163 <222> LOCATION: (2)..(4)  
164 <223> OTHER INFORMATION: Asp and Dpr are bound together to form a cycle  
166 <220> FEATURE:  
167 <221> NAME/KEY: MISC\_FEATURE  
168 <222> LOCATION: (5)..(5)  
169 <223> OTHER INFORMATION: X is Dpr (i.e. 2,3-diaminopropionic acid)  
171 <400> SEQUENCE: 5  
W--> 173 Asp Asp Trp Phe Xaa Leu  
174 1 5  
177 <210> SEQ ID NO: 6  
178 <211> LENGTH: 6  
179 <212> TYPE: PRT  
180 <213> ORGANISM: Artificial Sequence  
182 <220> FEATURE:  
183 <223> OTHER INFORMATION: bicyclic hexapeptide  
186 <220> FEATURE:  
187 <221> NAME/KEY: SITE  
188 <222> LOCATION: (1)..(6)  
189 <223> OTHER INFORMATION: Asp and Leu are bound together to form a cycle  
191 <220> FEATURE:  
192 <221> NAME/KEY: SITE  
193 <222> LOCATION: (2)..(5)  
194 <223> OTHER INFORMATION: Asp and Dpr are bound together to form a cycle  
196 <220> FEATURE:  
197 <221> NAME/KEY: MISC\_FEATURE  
198 <222> LOCATION: (5)..(5)  
199 <223> OTHER INFORMATION: X is Dpr (i.e. 2,3-diaminopropionic acid)  
201 <400> SEQUENCE: 6  
W--> 203 Asp Asp Trp Phe Xaa Leu

## RAW SEQUENCE LISTING

DATE: 07/03/2006

PATENT APPLICATION: US/10/537,731

TIME: 11:56:39

Input Set : E:\3874 PTUS sequence listing.txt

Output Set: N:\CRF4\07032006\J537731.raw

```
204 1          5
207 <210> SEQ ID NO: 7
208 <211> LENGTH: 6
209 <212> TYPE: PRT
210 <213> ORGANISM: Artificial Sequence
212 <220> FEATURE:
213 <223> OTHER INFORMATION: bicyclic glycopeptide
216 <220> FEATURE:
217 <221> NAME/KEY: SITE
218 <222> LOCATION: (1)..(6)
219 <223> OTHER INFORMATION: Asp and Leu are bound together to form a cycle
221 <220> FEATURE:
222 <221> NAME/KEY: CARBOHYD
223 <222> LOCATION: (1)..(1)
224 <223> OTHER INFORMATION: Asp is bound to
225     2-acetamide-3,4,6-tri-O-acetyl-2-deoxy-beta-D-glucopyranosylamine
227 <220> FEATURE:
228 <221> NAME/KEY: SITE
229 <222> LOCATION: (2)..(5)
230 <223> OTHER INFORMATION: Asp and Dpr are bound together to form a cycle
232 <220> FEATURE:
233 <221> NAME/KEY: MISC_FEATURE
234 <222> LOCATION: (5)..(5)
235 <223> OTHER INFORMATION: X is Dpr (i.e. 2,3-diaminopropionic acid)
237 <400> SEQUENCE: 7
W--> 239 Asp Asp Trp Phe Xaa Leu
240 1          5
243 <210> SEQ ID NO: 8
244 <211> LENGTH: 6
245 <212> TYPE: PRT
246 <213> ORGANISM: Artificial Sequence
248 <220> FEATURE:
249 <223> OTHER INFORMATION: bicyclic glycopeptide
252 <220> FEATURE:
253 <221> NAME/KEY: SITE
254 <222> LOCATION: (1)..(6)
255 <223> OTHER INFORMATION: Asp and Leu are bound together to form a cycle
257 <220> FEATURE:
258 <221> NAME/KEY: CARBOHYD
259 <222> LOCATION: (1)..(1)
260 <223> OTHER INFORMATION: Asp is bound to 2-acetamide-2-deoxy-beta-D-
glucopyranosylamine
262 <220> FEATURE:
263 <221> NAME/KEY: SITE
264 <222> LOCATION: (2)..(5)
265 <223> OTHER INFORMATION: Asp and Dpr are bound together to form a cycle
267 <220> FEATURE:
268 <221> NAME/KEY: MISC_FEATURE
269 <222> LOCATION: (5)..(5)
270 <223> OTHER INFORMATION: X is Dpr (i.e. 2,3-diaminopropionic acid)
```



## RAW SEQUENCE LISTING

DATE: 07/03/2006

PATENT APPLICATION: US/10/537,731

TIME: 11:56:39

Input Set : E:\3874 PTUS sequence listing.txt

Output Set: N:\CRF4\07032006\J537731.raw

272 <400> SEQUENCE: 8  
W--> 274 Asp Asp Trp Phe Xaa Leu  
275 1 5  
278 <210> SEQ ID NO: 9  
279 <211> LENGTH: 4  
280 <212> TYPE: PRT  
281 <213> ORGANISM: Artificial Sequence  
283 <220> FEATURE:  
284 <223> OTHER INFORMATION: tetrapeptide  
287 <220> FEATURE:  
288 <221> NAME/KEY: BINDING  
289 <222> LOCATION: (1)..(1)  
290 <223> OTHER INFORMATION: Trp is bound to a benzyloxycarbonyl group  
292 <220> FEATURE:  
293 <221> NAME/KEY: MISC\_FEATURE  
294 <222> LOCATION: (3)..(3)  
295 <223> OTHER INFORMATION: X is Dpr (i.e. 2,3-diaminopropionic acid)  
297 <220> FEATURE:  
298 <221> NAME/KEY: BINDING  
299 <222> LOCATION: (3)..(3)  
300 <223> OTHER INFORMATION: Dpr is bound to a tert-butoxycarbonyl group  
302 <220> FEATURE:  
303 <221> NAME/KEY: MOD\_RES  
304 <222> LOCATION: (4)..(4)  
305 <223> OTHER INFORMATION: METHYLATION  
307 <400> SEQUENCE: 9  
W--> 309 Trp Phe Xaa Leu  
310 1  
313 <210> SEQ ID NO: 10  
314 <211> LENGTH: 4  
315 <212> TYPE: PRT  
316 <213> ORGANISM: Artificial Sequence  
318 <220> FEATURE:  
319 <223> OTHER INFORMATION: tetrapeptide  
322 <220> FEATURE:  
323 <221> NAME/KEY: MISC\_FEATURE  
324 <222> LOCATION: (3)..(3)  
325 <223> OTHER INFORMATION: X is Dpr (i.e. 2,3-diaminopropionic acid)  
327 <220> FEATURE:  
328 <221> NAME/KEY: BINDING  
329 <222> LOCATION: (3)..(3)  
330 <223> OTHER INFORMATION: Dpr is bound to a tert-butoxycarbonyl group  
332 <220> FEATURE:  
333 <221> NAME/KEY: MOD\_RES  
334 <222> LOCATION: (3)..(3)  
335 <223> OTHER INFORMATION: METHYLATION  
337 <400> SEQUENCE: 10  
W--> 339 Trp Phe Xaa Leu  
340 1

RAW SEQUENCE LISTING ERROR SUMMARY      DATE: 07/03/2006  
PATENT APPLICATION: US/10/537,731      TIME: 11:56:40

Input Set : E:\3874 PTUS sequence listing.txt  
Output Set: N:\CRF4\07032006\J537731.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:1; Xaa Pos. 4 ✓  
Seq#:2; Xaa Pos. 4 ✓  
Seq#:3; Xaa Pos. 4 ✓  
Seq#:4; Xaa Pos. 5 ✓  
Seq#:5; Xaa Pos. 5 ✓  
Seq#:6; Xaa Pos. 5 ✓  
Seq#:7; Xaa Pos. 5 ✓  
Seq#:8; Xaa Pos. 5 ✓  
Seq#:9; Xaa Pos. 3 ✓  
Seq#:10; Xaa Pos. 3 ✓  
Seq#:11; Xaa Pos. 4 ✓

## VERIFICATION SUMMARY

DATE: 07/03/2006

PATENT APPLICATION: US/10/537,731

TIME: 11:56:40

Input Set : E:\3874 PTUS sequence listing.txt

Output Set: N:\CRF4\07032006\J537731.raw

L:9 M:270 C: Current Application Number differs, Replaced Current Application Number  
L:10 M:271 C: Current Filing Date differs, Replaced Current Filing Date  
L:42 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:0  
L:77 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:0  
L:107 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:0  
L:138 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4 after pos.:0  
L:173 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:5 after pos.:0  
L:203 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:6 after pos.:0  
L:239 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:7 after pos.:0  
L:274 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:8 after pos.:0  
L:309 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:9 after pos.:0  
L:339 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10 after pos.:0  
L:375 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:11 after pos.:0